Remarks

Upon entry of the amendment, claims 19 and 25-76 will be pending. Claims 19, 28, 30, 34, 36, 39, 41, 44, 46, 49, 51, 54, 56, 59, 61, 64, 66, 69, 71, 74 and 76 have been amended. Claims 1, 11, 13, 17-18, 20, 22-24 and 77 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the canceled subject matter in continuing applications. No new matter has been introduced.

I. Restriction Requirement and Request for Rejoinder of Claim 19

Applicants acknowledge that the Examiner's restriction requirement has been made final. The Examiner has withdrawn claims 1, 13, 17-18, 20, 22-24 and 77 from consideration. As pointed out above, claims to the non-elected inventions have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the canceled subject matter in continuing applications.

In the event that the claims of elected Group II are found allowable, Applicants respectfully request that the Examiner rejoin claim 19 (drawn to a method of diagnosis by detecting a protein).

II. Rejection under 35 U.S.C. § 101

Claims 11 and 25-76 have been rejected under 35 U.S.C. § 101 as allegedly not being supported by a specific, substantial and credible utility or, in the alternative, a well-established utility. *See*, Paper No. 11, at page 4. Specifically, the Examiner asserts at page 5, line 1-7 of Paper No. 11:

> The claimed polypeptides are not supported by a specific utility because the utilities disclosed for these polypeptides are generally applicable to all nucleic acids. The specification (see, for example, pages 78-79) teaches that the claimed polypeptides are 'primarily' expressed in activated helper T-cells and therefore can be used to identify the tissue or cell type present in a biological sample. However, expression of a polypeptide in activated helper T-cells is not considered to be a specific utility since there are a multitude of other polypeptides that are also expressed in activated helper T-cells.

Applicants respectfully disagree and traverse.

Preliminarily, Applicants respectfully point out that claim 11 has been canceled without prejudice or disclaimer. Therefore, the rejection as applied to claim 11 is moot. Applicants respectfully request that the rejection of claim 11 under 35 U.S.C. § 101 be withdrawn.

Additionally, Applicants point out that pending claims 25-76 are directed to Gene No. 33 whose polynucleotide sequence (SEQ ID NO:43) encodes the claimed polypeptide (SEQ ID NO:139). *See*, Provisional Election With Traverse submitted July 26, 2002 at pages 9-10. Based on the statements made by the Examiner, Applicants respectfully point out that the Examiner has mistakenly addressed her utility assessment with reference to polypeptides encoded by Gene No. 43. *See* Paper No. 11, pages 5-6. For example, the Examiner states that "the specification teaches that the claimed polypeptides are 'primarily' expressed in activated T-helper cells" and that the claimed polypeptides share sequence homology with the P195 protein of *Plasmodium falciparium*. *See*, Paper No. 11, page 5. Thus, Applicants respectfully point out that the rejection under 35 U.S.C. § 101 cannot be maintained as the Examiner's entire reasoning for imposing the rejection is based on disclosure in the specification for a non-elected gene (Gene No. 43). Therefore, Applicants respectfully request that the rejection of claims 25-76 be reconsidered and withdrawn.

While Applicants maintain that the rejection under 35 U.S.C. § 101 should be withdrawn, Applicants have the following comments in regard to the elected polypeptides encoded by Gene No. 33.

Applicants have set forth in the specification statements that clearly provide specific, substantial and credible utility. For example, Applicants disclose that the gene, which encodes the polypeptide of the invention (SEQ ID NO:139), is primarily found in B-cell lymphoma. Based in part on this tissue expression, Applicants assert that the claimed polypeptide (SEQ ID NO:139) encoded by Gene No. 33 can be used as a diagnostic probe in detecting, for example, diseases of the immune or hematopoietic systems, including cancers such as B-cell lymphoma (*See*, specification at page 59, line 36 to page 60, line 2).

These asserted utilities are specific and substantial. First, the disclosed uses of the polypeptides of the invention are not generally applicable to all proteins. For instance, all proteins are not useful in providing immunological probes for differential identification of B-cell lymphoma (*i.e.*, useful as a B-cell lymphoma diagnostic). Second, the use of the claimed polypeptides in the detection of a specific disease such as B-cell lymphoma is certainly a "real world" use.

In addition, Applicants respectfully point out that the asserted utilities are credible. In support of the credibility of these assertions, Applicants have submitted herewith an executed declaration under 37 C.F.R. § 1.132 of Dr. George Komatsoulis, from Human Genome Sciences, Inc. The executed declaration under 37 C.F.R. § 1.132 indicates that the expression of the polynucleotide SEQ ID NO:43 was assessed in hundreds of human tissues, including

cancerous tissue (*e.g.*, B-cell lymphoma tissue), as well as many other "normal" (*i.e.*, non-cancerous) blood cells (*e.g.*, T cells, B cells, monocytes). Based on this assessment, no expression was observed in "normal" blood cells. In contrast, expression was observed in B-cell lymphoma tissue. Thus, given this differential expression in diseased versus normal blood cells, the polypeptide encoded by SEQ ID NO:43 would be useful as a specific diagnostic marker for B-cell lymphoma in a mixed blood cell population as asserted in the specification.

Furthermore, Applicants submit herewith, as Exhibits A-C, evidence further supporting the credibility of using the claimed polypeptide in the diagnosis of B-cell lymphoma. For instance, a search of the Genbank database reveals that SEQ ID NO:43, the polynucleotide that encodes SEQ ID NO:139, is located on chromosome 12, specifically the 12p arm of chromosome 12. *See* Genbank Accession No. AC004804 (first ten pages only) and the BLAST comparison between SEQ ID NO:43 (Gene No. 33) and Genbank Accession No. AC004804, submitted collectively as Exhibit A. Importantly, Exhibit A demonstrates the nexus between the 12p arm of chromosome 12 and B-cell lymphomas which is well recognized within the scientific community. *See* Jonveaux *et al.* (1991) Hematol Pathol 5:21-26 and Dierlamm *et al.* (1997) Genes Chromosomes Cancer 20:155-166 (Abstracts only; submitted herewith as Exhibits B-C, respectively). These data, taken together, provide further evidence that there is a credible link between the gene encoding SEQ ID NO:139 of the claimed invention and B-cell lymphoma. Thus, based on the totality of evidence of record, Applicants submit that one of ordinary skill in the art would find it, more likely than not, true that the asserted utilities for the claimed invention are credible.

As pointed out above, the Examiner has assessed the utility of the claimed polypeptides based on the disclosure of a non-elected gene, thus, Applicants respectfully submit that the rejection of claims 25-76 under 35 U.S.C. § 101 should be withdrawn. Nonetheless, in view of the evidence and reasoning provided above, Applicants submit that the utility asserted in the specification for secreted protein HBJFE12 is indeed specific, substantial and credible.

III. Rejections Under 35 U.S.C. § 112, First Paragraph

A. The Examiner has also rejected claims 11 and 25-76 under 35 U.S.C. § 112, first paragraph, as allegedly failing to adequately teach how to use the instant invention. Specifically, the Examiner asserts:

> [s]ince the claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above, one of skill in the art would not know how to use the claimed invention.

See, Paper No. 11, page 7, paragraph 5.

Applicants respectfully disagree and traverse.

Preliminarily, Applicants respectfully point out that claim 11 has been canceled without prejudice or disclaimer, thereby rendering the rejection to claim 11 moot. Applicants respectfully request withdrawal of the rejection as applied to claim 11.

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, Applicants submit that the claimed invention is supported by a specific, substantial, and credible utility. The Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. § 101 rejection is proper." M.P.E.P. § 2107(IV) at 2100-28 (Rev.1, Feb. 2000). Therefore, since the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejection of claims 25-76 under 35 U.S.C. § 112, first paragraph, based on lack of utility of the claimed invention, should be withdrawn.

B. The Examiner has also rejected claims 11, 31-36, 42-46, 52-56, 62-66, and 72-76 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, and with which it is most nearly connected, to make and/or use the invention. More specifically, the Examiner asserts:

> [t]he specification has not adequately taught how to make and use the polypeptides encoded by the HBJEF12 cDNA contained in ATCC Deposit No. 209177 because the specification has not fulfilled the requirements for the deposit of this cell line. ... [t]he specification does not provide the required assurances that all of the conditions of 37 CFR sections 1.801-1.809 have been met.

See, Paper No. 11, pages 7-8, paragraph 5.

Applicants respectfully disagree and traverse.

Preliminarily, Applicants respectfully point out that claim 11 has been canceled without prejudice or disclaimer, thereby rendering the rejection to claim 11 moot. Applicants respectfully request withdrawal of the rejection as applied to claim 11.

Applicants respectfully point out that they are in full compliance of the requirements of 37 C.F.R. §§ 1.801-1.809. For instance, the specification, as set forth in 37 C.F.R. §

1.809(d), clearly recites the deposit number by accession number, as well as, provides all other necessary information. Specifically, on page 162, Table 1, row 7, the specification recites the ATCC Deposit number for the cDNA encoding the polypeptides of SEQ ID NO:139 (ATCC Deposit No. 209177) and the deposited date (July 24, 1997).

In addition, the specification clearly discloses that ATCC Deposit No. 209177 has been deposited under the terms of the Budapest Treaty on International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. *See*, pages 3-4, bridging paragraph. Therefore, Applicants respectfully submit that the specification is in compliance with C.F.R. §§ 1.801-1.809, but if the Examiner would like additional description of the deposit, please advise the Applicants accordingly.

Further, as attorney for the above-identified Applicants in the above-identified patent application, I hereby declare and state that:

1. ATCC Deposit No. 209177 containing DNA Plasmid No. PS044 was deposited with the American Type Culture Collection (ATCC), now located at 10801 University Boulevard, Manassas, VA 20110-2209, U.S.A. on July 24, 1997, in compliance with the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure.

2. I hereby assure the United States Patent and Trademark Office and the public that (a) all restrictions on the availability to the public of a sample of the above-mentioned deposited plasmid will be irrevocably removed upon issuance of a United States patent of which the plasmid(s) is a subject; (b) the above-mentioned deposited plasmids will be maintained for a period of at least five years after the most recent request for the furnishing of a sample of the plasmid was received by the ATCC and, in any case for a period of at least 30 years after the date of deposit or for the enforceable life of such patent, whichever is longer; (c) should the above-mentioned deposited plasmid become non-viable or mutated or otherwise incapable of being furnished by the depository upon request due to the condition of the deposit, the plasmid will be replaced by the Applicants; and (d) access to the above-mentioned deposited plasmid will be available to the Commissioner during the pendency of the patent application or to one determined by the Commissioner to be entitled to such plasmid under 37 C.F.R. § 1.14 and 35 U.S.C. § 122.

In view of the above, Applicants submit that the rejection under 35 U.S.C. § 112, first

paragraph, has been obviated. Accordingly, Applicants respectfully request that the rejection of claims 31-36, 42-46, 52-56, 62-66, and 72-76 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

C. Claims 11, 25, 29-32, 34-71 and 74 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. In particular, the Examiner asserts:

> [t]he specification has not identified any variants having similar activity or having more or less activity than the polypeptide of SEQ ID NO:139. With respect to polypeptides comprising fragments of SEQ ID NO;139, the claims are inclusive of polypeptides containing an unstated number of amino acids from SEQ ID NO:139 (e.g., 1, 2, 3, etc. amino acids) and containing flanking sequences of unknown identity and length. The specification has not exemplified any variants containing only a portion of SEQ ID NO:139 and has not adequately described the sequences which may flank SEQ ID NO:139 and fragments thereof. ... [w]hile polypeptides consisting of SEQ ID NO:139 and polypeptides consisting of amino acids 19-47 of SEQ ID NO:139 meet the written description requirements of 35 U.S.C. 112, first paragraph, the specification does not disclose and fully characterize the genus of any variant of the protein of SEQ ID NO:139.

See, Paper No 11, page 9.

Applicants respectfully disagree and traverse.

Preliminarily, Applicants respectfully point out that claim 11 has been canceled without prejudice or disclaimer, thereby rendering the rejection to claim 11 moot. Applicants respectfully request withdrawal of the rejection as applied to claim 11.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. Further, the Federal Circuit recently re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [they] invented what is claimed,'" *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 54 U.S.P.Q.2d 1227 (Fed. Cir. 2000). While the applicant must "blaze marks on trees," rather than "simply [provide] the public with a forest of trees," an Applicant is not required to explicitly describe each of the trees in the forest. *See Unocal*, 208 F.3d at 1000. *See also*

M.P.E.P. § 2163.02 ("The subject matter of the claim need not be described literally (*i.e.*, using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement."). The Court emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification, rather than whether the specific embodiments had been explicitly described or exemplified. Indeed, as the court noted, "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Unocal*, 208 F.3d at 1001 (emphasis added).

Applicants respectfully disagree with the Examiner and submit that one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims in the present application as filed. Applicants further submit that the Examiner has underestimated both the teaching of the present application and the level of skill in the art on the priority date of the present application.

Applicants recognize that the Examiner is in part relying on language regarding a "representative number" of a claimed genus set forth in *Regents of the University of California v. Eli Lilly & Co.*, (119 F.3d 1559, 1569, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997)) and incorporated into the Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶ 1 "Written Description" Requirement ("Guidelines"), when reciting the procedures followed in analyzing whether the description requirement for each of the claims at issue is satisfied. However, even assuming, *arguendo*, that the Guidelines comport with the law, the Guidelines also define a "representative number" as "an inverse function of the skill and knowledge of the art." (*See* Guidelines at Page 1106.) Applicants note that the level of skill in the art on the priority date of the present application was very high.

Furthermore, the central issue in *Eli Lilly* involved claims to mammalian cDNAs encoding insulin, which were supported in the specification only by the nucleotide sequence for the rat insulin gene. The Federal Circuit found the claims to human insulin lacked written description because the claims defined only a result or function. The court held that a result or function will satisfy the written description requirement *only if* correlated to a description of structural features of the claimed invention. According to the court, a sufficient written description must allow the skilled artisan to "visualize or recognize the identity of the members of the genus." *Id.*

Unlike the situation in *Eli Lilly*, the presently rejected claims do not claim polynucleotides by result or function. Applicants submit that, one skilled in the art, enlightened by teachings of the present application, could readily envision countless polypeptide sequences that comprise the specified polypeptides. For example, the skilled

artisan could clearly envision each of the polypeptides that are 90% or 95% identical to the polypeptide of SEQ ID NO:139 as a polypeptide with, *e.g.*, 1-5 conservative amino acid substitutions along its length. Indeed, nothing more than a basic knowledge of the genetic code and what is described in the specification would be required for the skilled artisan to identify every single one of the polypeptides that are 90% or 95% identical to the amino acid sequence of SEQ ID NO:139. Clearly, such knowledge is well within what is expected of the skilled artisan. Further, the instant claims do not require the claimed sequences to possess any particular activity or characteristic beyond the described sequence, and the subject matter of what is claimed is fully supported by the specification. 35 U.S.C. § 112 requires no more. *See Unocal*, 208 F.3d at 1000; M.P.E.P. § 2163.02.

Accordingly, from reading the specification, the skilled person would immediately recognize that, at the time the specification was filed, the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563); namely, a genus of proteins comprising polypeptides with 90% or 95% identity to the amino acids of SEQ ID NO:139 (or of the polypeptide encoded by the cDNA of the claimed deposit). Therefore, the specification contains an adequate written description of the claimed polypeptides.

In view of the above, Applicants respectfully assert that the Examiner has failed to meet the required burden in presenting evidence or reasons why those skilled in the art would not recognize the claimed invention from the disclosure. Moreover, the specification conveys with reasonable clarity that Applicants were in possession of the claimed invention. Therefore, Applicants submit that the claims fully meet the written description requirements of 35 U.S.C. § 112, first paragraph, and respectfully request that the Examiner's rejection of the claims 25, 29-32, 34-71 and 74 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

IV. Rejections Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 28, 30, 34, 36, 39, 41, 44, 46, 49, 51, 54, 56, 61, 64, 66, 69, 71, 74 and 76 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. *See*, Paper No 11, page 11, paragraph 7.

A. In regards to the rejection of claims 30, 36, 41, 46, 51, 56, 61, 66, 71 and 76, the Examiner alleges on paragraph 7 of the Office Action:

> Claims 30, 36, 41, 46, 51, 56, 61, 66, 71 and 76 are indefinite over the recitation of 'expressing the protein of claim _ by a cell.' It is generally accepted that a nucleic acid is expressed by a cell. However, it is unclear as to what is intended to be meant by a expressing a protein by a cell.

Applicants respectfully disagree; however, solely to expedite prosecution, the rejected claims have been amended to replace the phrase "expressing the protein of claim _ by a cell" with "synthesizing the protein of claim _ in a cell." Applicants believe that the amendment of the claims obviates the Examiner's rejection of claims 30, 36, 41, 46, 51, 56, 61, 66, 71 and 76 under 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 30, 36, 41, 46, 51, 56, 61, 66, 71 and 76 under 35 U.S.C. § 112, second paragraph.

B. The Examiner has further rejected claims 28, 34, 39, 44, 49, 54, 59, 64, 69 and 74 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite due to the recitation of the phrase "which further comprises a polypeptide sequence heterologous to SEQ ID NO:139." Specifically, the Examiner asserts at page 12 of Paper No. 11:

> [t]his recitation does not further limit the claims from the claims from which they depend since this limitation adds a new element to the claimed polypeptides. Furthermore, it is unclear as to what is intended to be encompassed by a sequence heterologous to SEQ ID NO:139.

Applicants respectfully disagree and traverse.

Applicants assert that claims 28, 34, 39, 44, 49, 54, 59, 64, 69 and 74 are proper dependent claims in that they refer back to and <u>further limit</u> the independent claims to which they depend. For example, since claims 28, 34, 39, 44, 49, 54, 59, 64, 69 and 74 recite "a polypeptide sequence heterologous to SEQ ID NO:139," the subject matter encompassed by said dependent claims could <u>not</u> include the polypeptides of SEQ ID NO:139 fused to itself as, *e.g.*, homodimers. However, this subject matter <u>would</u> be encompassed by independent claims 25, 31, 37, 42, 47, 52, 57, 62, 67 and 72. In other words, the subject matter of the independent claims could include either a heterologous sequence or SEQ ID NO:139 itself fused to the polypeptide of SEQ ID NO:139. On the other hand, the subject matter of the dependent claims must include a <u>heterologous</u> sequence fused to the polypeptide of SEQ ID NO:139. Accordingly, the dependent claims refer back and further limit the independent claims. Thus, these dependent claims as written, do further limit the claim upon which they depend.

Nonetheless, Applicants have amended claims 28, 34, 39, 44, 49, 54, 59, 64, 69 and 74 to read "which is fused to a polypeptide sequence heterologous to SEQ ID NO:139." Applicants believe that the amendments unambiguously further limits the claim from which they depend. Support of fusion proteins can be found, for example, at Example 9 of the specification. *See*, pages 218-219. Applicants respectfully request that the rejection of claims 28, 34, 39, 44, 49, 54, 59, 64, 69 and 74 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

V. Rejections Under 35 U.S.C. § 102(e)

Claim 11 has been rejected by the Examiner under 35 U.S.C. § 102(e) as being anticipated by Veenstra *et al.* (U.S. Patent No. 5,882,879). Specifically, the Examiner asserts that the Veenstra *et al.* reference discloses a polypeptide which "comprises" a fragment of instant SEQ ID NO:139.

Applicants respectfully disagree; however, Applicants respectfully point out that claim 11 has been canceled without prejudice or disclaimer, thereby rendering the rejection to claim 11 moot. Applicants respectfully request that the rejection under 35 U.S.C. § 102(e) be withdrawn.

Conclusion

Applicants respectfully request the remarks of the present response be entered and made of record in the present application. In view of the foregoing remarks, Applicants believe they have fully addressed the Examiner's concerns and that this application is now in condition for allowance. An early notice to that effect is urged. A request is made to the Examiner to call the undersigned at the phone number provided below if any further action by Applicants would expedite allowance of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,

Date: January 10, 2003

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KKH/JMM/JL/SA/vr

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: **Ruben** *et al.*

Application Serial No.: 09/774,639 Art Unit: 1634

Filed: February 1, 2001 Examiner: Myers, C.

For: Secreted Protein HBJFE12 (as amended) Attorney Docket No.: PZ013P1C1

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Changes to the application follow. Text that has been inserted is underlined and text that has been deleted is struck through.

In the Claims:

Please cancel claims 1, 11, 13, 17-18, 20, 22-24 and 77 without prejudice or disclaimer.

Please amend the following claims:

19. (Once Amended) A method of diagnosing a pathological condition or susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of claim 25 ~~11~~ in a biological sample; and

(b) diagnosing a pathological condition or susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

28. (Once Amended) The isolated polypeptide of claim 25 which is fused to ~~further comprises~~ a polypeptide sequence heterologous to SEQ ID NO:139.

30. (Once Amended) An isolated protein produced by the method comprising:

(a) synthesizing ~~expressing~~ the polypeptide of claim 25 in ~~by~~ a cell; and

(b) recovering said protein.

34. (Once Amended) The protein of claim 31 which is fused to ~~further comprises~~ a polypeptide sequence heterologous to SEQ ID NO:139.

36. (Once Amended) An isolated protein produced by the method comprising:

(a) synthesizing ~~expressing~~ the protein of claim 31 in ~~by~~ a cell; and

(b) recovering said protein.

39. (Once Amended) The isolated first polypeptide of claim 37 which is fused to ~~further comprises~~ a polypeptide sequence heterologous to SEQ ID NO:139.

41. (Once Amended) An isolated protein produced by the method comprising:

(a) synthesizing ~~expressing~~ the first polypeptide of claim 37 in ~~by~~ a cell; and

(b) recovering said protein.

44. (Once Amended) The isolated first polypeptide of claim 42 which is fused to ~~further comprises~~ a polypeptide sequence heterologous to SEQ ID NO:139.

46. (Once Amended) An isolated protein produced by the method comprising:

(a) synthesizing ~~expressing~~ the first polypeptide of claim 42 in ~~by~~ a cell; and

(b) recovering said protein.

49. (Once Amended) The isolated first polypeptide of claim 47 which is fused to ~~comprises~~ a heterologous polypeptide sequence.

51. (Once Amended) An isolated protein produced by the method comprising:

(a) synthesizing ~~expressing~~ the isolated first polypeptide of claim 47 in ~~by~~ a cell; and

(b) recovering said protein.

54. (Once Amended) The isolated first polypeptide of claim 52 which is fused to ~~further comprises~~ a polypeptide sequence heterologous to SEQ ID NO:139.

56. (Once Amended) An isolated protein produced by the method comprising:

(a) synthesizing ~~expressing~~ the isolated first polypeptide of claim 52 in ~~by~~ a cell; and

(b) recovering said protein.

59. (Once Amended) The isolated polypeptide of claim 57 which is fused to ~~further comprises~~ a polypeptide sequence heterologous to SEQ ID NO:139.

61. (Once Amended) An isolated protein produced by the method comprising:

(a) synthesizing ~~expressing~~ the polypeptide of claim 57 in a cell; and

(b) recovering said protein.

64. (Once Amended) The isolated protein of claim 62 which is fused to ~~further comprises~~ a polypeptide sequence heterologous to SEQ ID NO:139.

66. (Once Amended) An isolated protein produced by the method comprising:

(a) synthesizing ~~expressing~~ the protein of claim 62 in ~~by~~ a cell; and

(b) recovering said protein.

69. (Once Amended) The isolated protein of claim 67 which is fused to ~~further comprises~~ a polypeptide sequence heterologous to SEQ ID NO:139.

71. (Once Amended) An isolated protein produced by the method comprising:

(a) synthesizing ~~expressing~~ the protein of claim 67 in ~~by~~ a cell; and

(b) recovering said protein.

74. (Once Amended) The isolated protein of claim 72 which is fused to ~~further comprises~~ a polypeptide sequence heterologous to SEQ ID NO:139.

76. (Once Amended) An isolated protein produced by the method comprising:

(a) synthesizing ~~expressing~~ the protein of claim 72 in ~~by~~ a cell; and

(b) recovering said protein.